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LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG,
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European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: PURIFIED AND ISOLATED PLATELET CALCIUM CHANNEL NUCLEIC ACIDS AND POLYPEPTIDES AND THERAPEUTIC AND SCREENING METHODS USING SAME

(57) Abstract: Isolated and purified platelet voltage dependent calcium channel (VDCC), α_1 subunit polypeptides, and nucleic acid molecules encoding the same. Recombinant host cells, recombinant nucleic acids and recombinant proteins are also disclosed, along with methods of producing each. Isolated and purified antibodies to platelet VDCC α_1 subunit polypeptides have biological activity in calcium transport. Thus, therapeutic and diagnostic methods involving this activity are also disclosed.



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INTERNATIONAL SEARCH REPORT

Int. Application No
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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C07K14/705 C07K16/28 G01N33/53 C12Q1/68
G01N33/68 A61K38/17 A61K48/00 A61K31/70 C12N15/11
A61K39/395 A01K67/027

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K G01N C12Q A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EMBASE, MEDLINE, EPO-Internal, EMBL, SEQUENCE SEARCH

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL 'Online! EBI; 16 December 1994 (1994-12-16) HOGAN, K. ET AL.: "Human dihydroxypyridine-sensitive L-type calcium channel alpha-1 subunit (CACNL1A3) mRNA" Database accession no. L33798 XP002224388 abstract	1-11, 13-41, 43-52, 55-62
X	-& HOGAN, K. ET AL.: "Cloning of the human skeletal muscle alpha-1 subunit of dihydroxypyridine-sensitive L-type calcium channel (CACNL1A3)" GENOMICS, vol. 24, no. 3, - 1 December 1994 (1994-12-01) pages 608-609, XP000647669 the whole document --- -/--	1-11, 13-41, 43-52, 55-62

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

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International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL 'Online! EBI; 17 November 1992 (1992-11-17) CHAUDHARI, N.: "Mus musculus dihydroxypyridine sensitive skeletal muscle calcium channel mRNA" Database accession no. L06234 XP002224389 abstract</p>	<p>1-11, 13-41, 43-52, 55-62</p>
X	<p>-& CHAUDHARI, N.: "A single nucleotide deletion in the skeletal muscle-specific calcium channel transcript of muscular dysgenesis (mdg) mice" J. BIOL. CHEM., vol. 267, no. 36, - 25 December 1992 (1992-12-25) pages 25636-25639, XP002224386 the whole document</p>	<p>1-11, 13-41, 43-52, 55-62</p>
X	<p>--- US 5 686 241 A (BRENNER ROBERT ET AL) 11 November 1997 (1997-11-11)</p> <p>figures 1A-F</p>	<p>1-11, 13-41, 43-52, 55-62</p>
X	<p>--- HOGAN K ET AL: "The structure of the gene encoding the human skeletal muscle alpha 1 subunit of the dihydropyridine-sensitive L-type calcium channel (CACNL1A3)." GENOMICS. UNITED STATES 1 FEB 1996, vol. 31, no. 3, 1 February 1996 (1996-02-01), pages 392-394, XP002224387 ISSN: 0888-7543 the whole document</p>	<p>1-11, 13-41, 43-52, 55-62</p>
X	<p>--- TANG S ET AL: "MOLECULAR LOCALIZATION STUDIES OF THE DIHYDROPYRIDINE (DHP) BINDING SITE IN THE CARDIAC L-TYPE VOLTAGE DEPENDENT CA2+ CHANNEL (L-VDCC)A1 SUBUNIT REVEAL MOTIF IV S3 TO IV S6 AS ESSENTIAL" BIOPHYSICAL JOURNAL, NEW YORK, US, US, vol. 64, no. 2, 1993, page A06 XP000604115 ISSN: 0006-3495 abstract</p>	<p>1,3-9, 13-18, 21-41, 43-52, 55-62</p>
X	<p>--- US 5 429 921 A (HARPOLD MICHAEL M ET AL) 4 July 1995 (1995-07-04)</p> <p>* see SEQ ID NO: 1, relevant for SEQ ID NO: 3 of the present application *</p> <p>--- -/--</p>	<p>1-11, 13-41, 43-52, 55-62</p>

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/50328

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL/GENBANK/DBJ 'Online! 29 March 1995 (1995-03-29) IHARA, YU ET AL.: "Rat rCACN4A mRNA for L-type voltage dependent calcium channel alpha 1 subunit" retrieved from EBI, accession no. D38101 XP002238191 * relevant for SEQ ID NO: 3 *</p> <p>abstract</p> <p>---</p>	<p>1-11, 13-41, 43-52, 55-62</p>
X	<p>DATABASE EMBL/GENBANK/DBJ 'Online! 3 February 1992 (1992-02-03) SEINO, S. ET AL.: "Human neuroendocrine/beta-cell-type calcium channel alpha-1 subunit mRNA" retrieved from EBI, accession no. M83566 XP002238192 * relevant for SEQ ID NO: 3 *</p> <p>abstract</p> <p>---</p>	<p>1-11, 13-41, 43-52, 55-62</p>
X	<p>DATABASE EMBL/GENBANK/DBJ 'Online! 1 October 1996 (1996-10-01) IHARA, YU. ET AL. : "Voltage-dependent L-type calcium channel alpha-1D subunit (rat)" retrieved from EBI, accession no. P27732 XP002238193 * relevant for SEQ ID NO: 4 *</p> <p>abstract</p> <p>---</p>	<p>1-11, 13-41, 43-52, 55-62</p>
X	<p>WO 95 04822 A (SALK INST BIOTECH IND) 16 February 1995 (1995-02-16)</p> <p>* relevant for SEQ ID NO: 4 *</p> <p>page 126 -page 127</p> <p>-----</p>	<p>1-11, 13-41, 43-52, 55-62</p>

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/50328

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 42, 53-54
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
1, 2 (partially) 3-9, 10-11 (partially), 13-18, 19-20 (partially), 21-41, 43-52, 55-62

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: 1, 2 (partially), 3-9,
10-11 (partially), 13-18, 19-20 (partially),
21-41, 43-52, 55-62

An isolated and purified platelet voltage dependent calcium channel (VDCC) alpha-1 subunit polypeptide of SEQ ID NO: 2 and polynucleotide SEQ ID NO: 1 encoding such a polypeptide, an antibody which specifically binds to said polypeptide and a method for producing such an antibody, a hybridoma cell line which produces said antibody, a vector (host) comprising such a polynucleotide, a method (kit) for detecting the presence of said platelet VDCC alpha-subunit or polypeptide encoding said alpha-subunit, a method for to determine a mutation in said alpha-subunit, a method (kit) for detecting a polymorphism in said VDCC alpha-subunit, a method of screening candidate substances, a method of modulating VDCC alpha-1 subunit polypeptide, a method for modulating calcium transport in a cell, and a transgenic non-human organism having incorporated into its genome a nucleic acid molecule encoding VDCC alpha-1 subunit polypeptide.

Inventions 2-8: 2, 10-12, 19-20 (all partially)

An isolated and purified platelet voltage dependent calcium channel (VDCC) alpha-1 subunit polypeptide of SEQ ID NO: 4 and polynucleotide SEQ ID NO: 3 encoding such a polypeptide, and further polynucleotides SEQ ID NO: 5, 6, 7, 8, 28 and 29.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 42, 53-54

Present claims 42 and 53-54 relate to an extremely large number of possible recombinant cells and pharmaceutical compositions. In fact, the claims contain so many options and possibilities that a lack of clarity and conciseness within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Furthermore, said claims lack support and relate to matter which is not sufficiently disclosed.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/50328

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INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter national Application No

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